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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,089	10/04/2005	Mahesh Jayachandra	13860.1USWO	2753

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EXAMINER	
RIDER, LANCE W	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
12/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,089	JAYACHANDRA, MAHESH	
	Examiner	Art Unit	
	LANCE RIDER	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-22 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-22 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/11/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

The remarks and amendments filed on October 11th 2010 are acknowledged. Claims 1-5 and 7-22 are amended, claims 23-28 are canceled, withdrawn and claim 29 is newly added.

Response to arguments

Withdrawn Rejections

Receipt and consideration of Applicants' amended claim set and remarks filed on October 11th 2010 is acknowledged. Rejections and objections not reiterated from previous office actions are hereby withdrawn. The following rejections or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-20, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berde et al., U.S. Patent 6,046,187 in view of Stracher , et al., European Patent Application EP 0100673 as evidenced by Matsunari, I., et al., (Circulation, 2000) and Rosen, H., et al., (Stroke, 1998).

This rejection is MAINTAINED for the reasons of record set forth in the office action mailed on October 11th 2010 and for the reasons set forth below. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that the treatments of nerve damage cited use agents which treat through different mechanisms and would not be combinable.

In response to this argument, as stated in the previous action it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. In the instant case Berde teaches the use of procaine and methylprednisone for the treatment of nerve damage and pain, and Stracher teaches the use of leupeptin for the treatment of nerve damage. The idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**.

Applicant also argues that the Takatori reference (2006) shows that one of skill in the art would not combine procaine with leupeptin.

This argument raises several issues. The first issue is that applicant's are not arguing any teaching away in the art used. Given no such argument the combination appears to stand. Second the art cited is from 2006, well after the filing date of the application and all of the prior art of record. How could the skilled artisan at the time of the invention looked into the future to arrive at the assumption that using procaine would be a bad idea? Third even though Takatori indicates that some anesthetics may suppress nerve growth procaine is stated to have a small inhibitory effect and that large amounts of the drug were required to see any suppression, indicating the effect is concentration dependent and could be avoided or may not exist in vivo.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berde et al., U.S. Patent 6,046,187 in view of Stracher , et al., European Patent Application EP 0100673 as evidenced by Matsunari, I., et al., (Circulation, 2000) and Rosen, H., et al., (Stroke, 1998), as applied to claims 1-5, 7-20 and 22 above, and in further view of Young, W. et. al., (Current treatment for Human Spinal Cord Injury, web article included in IDS).

This rejection is MAINTAINED for the reasons of record set forth in the office action mailed on October 11th 2010 and for the reasons set forth below. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that the treatments of nerve damage cited use agents which treat through different mechanisms and would not be combinable.

In response to this argument, as stated in the previous action it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. In the instant case Berde teaches the use of procaine and methylprednisone for the treatment of nerve damage and pain, and Stracher teaches the use of leupeptin for the treatment of nerve damage. The idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**.

Applicant also argues that the Takatori reference (2006) shows that one of skill in the art would not combine procaine with leupeptin.

This argument raises several issues. The first issue is that applicant's are not arguing any teaching away in the art used. Given no such argument the combination appears to stand. Second the art cited is from 2006, well after the filing date of the application and all of the prior art of record. How could the skilled artisan at the time of the invention looked into the future to arrive at the assumption that using procaine would be a bad idea? Third even though Takatori indicates that some anesthetics may suppress nerve growth procaine is stated to have a small inhibitory effect and that large amounts of the drug were required to see any suppression, indicating the effect is concentration dependent and could be avoided or may not exist in vivo.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 29 is directed to a specific method of treating using specific amounts of specific drugs at specific sites which is not disclosed in the specification with enough clarity to direct the artisan to such an invention. Furthermore the applicant has created new dosage ranges not defined in the

specification such as the range of "about 200 ug/mL" where the specification only recites "about 200 ug/mL or more".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berde et al., U.S. Patent 6,046,187 in view of Stracher , et al., European Patent Application EP 0100673, Travis, et al., U.S. Patent 6,017,532, Saidi, et al., U.S. Patent 6,241,969, Josephson, I., et al., (Eur J. Pharm., 1976), and Del Bigio, M.R., et al. (Journal of Neurosurgery, 2001)

Berde teaches the use of a methylprednisone (a costicosteroid) and procaine (a local anesthetic) for the treatment of pain caused by nerve damage. (See claims 1, 8 and 16.) Berde teaches the use to treat peripheral nerves, somatic motor nerves, nerve plexuses, cranial nerves, and parasympathetic ganglia. Berde also teaches the treatment of circulatory dysfunctions using these compounds. (See column 21, paragraph 2, and column 18, paragraph 5.) Berde teaches that the compounds can be used locally or systemically. (See column 3, paragraph 2.) Berde teaches that the two agents can be administered together, before one another, or after one another. (See column 19, paragraph 5.) Berde also teaches that the agents can be used before or after pain or nerve injury occurs as either an anesthetic for surgeries or to treat pain occurring from an illness. (See column 18, paragraph 5, and column 20, paragraph 5.) Berde teaches the use of these compounds to treat peripheral nerves, somatic motor nerves, nerve plexuses, cranial nerves, and parasympathetic ganglia. Berde also teaches the treatment of circulatory dysfunctions using these compounds. (See column 21, paragraph 2, and column 18, paragraph 5.)

Berde does not teach the administration of a protease inhibitor to an "excitable tissue" or nerve.

Stracher teaches the administration of leupeptin in a pharmaceutically acceptable vehicle for the treatment of nerve damage. (See page 3, paragraph 3.) Stracher teaches that leupeptin can be administered at the site of the injured tissue and systemically by oral administration. (See page 18, claim 9, and page 6, paragraph 1.) Stracher teaches that the most efficient treatment with leupeptin is to treat the injured site as rapidly as possible, anywhere from immediately out to the 8 hours instantly claimed. Stracher teaches that leupeptin can be used to treat many types of nerve injuries such as spinal trauma, compression nerve injuries, endopathic neuropahy, and neuropraxis. (See page 4, paragraph 2.)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Berde and Stracher for many reasons. First it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. In the instant case Berde teaches the use of procaine and methylprednisone for the treatment of nerve damage and pain, and Stracher teaches the use of leupeptin for the treatment of nerve damage. The idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**. Second it would have been prima facie obvious to one of ordinary skill in the art to use a method to treat nerve pain as taught by Berde along with a treatment for nerve damage

in order to form an improved treatment which both repaired damaged nerves but also gave patients relief form pain at the same time.

Berde and Stracher do not teach using the specific protease inhibitor p-aminobenamidine.

Travis teaches that leupeptin and p-aminobenzamidine are art recognized equivalent cysteine protease inhibitors. (See column 3, lines 17-21)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to substitute one art recognized cysteine protease inhibitor for another in a method requiring such protease inhibitors. This is merely the substitution of one art recognized equivalent for another. The skilled artisan would have predicted that this substitution would function as both protease inhibitors were known to be useful for the same function as cysteine protease inhibitors.

Berde, Stracher, and Travis do not teach using the specific corticosteroid fluticasone propionate.

Saidi teaches that methylprednisolone and fluticasone propionate are art recognized equivalent corticosteriods. (See column 6, lines 8-31.)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to substitute one art recognized corticosteroid for another in a method requiring costicosteroids. This is merely the substitution of one art recognized equivalent for another. The skilled artisan would have predicted that this substitution would function as both compounds methylprednisolone and fluticasone propionate were known to be useful for the same function as costicosteroids.

Berde, Stracher, Travis, and Saidi do not teach using the specific local anesthetic phenytoin (diphenylhyatoin).

Josephson teaches that lidocaine, procaine, and phenytoin (diphenylhydatoin) are all art recognized equivalent local anesthetics. (See abstract.)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to substitute one art recognized local anesthetic for another in a method requiring local anesthetics. This is merely the substitution of one art recognized equivalent for another. The skilled artisan would have predicted that this substitution would function as both compounds phenytoin and procaine were known to be useful for the same function as local anesthetics.

Regarding the administration of the drug together or apart, Berde teaches the use of procaine (a local anesthetic) and methylprednisolone (a corticosteroid) without the inclusion of leupeptin (a protease inhibitor) disclosed in Stracher, so it is obvious from the prior art that the administration of the compounds has been performed separately. As both compounds are used to treat the same dysfunction, it would also logically flow that they could be used in combination. The treatment with different drug dosages and their administration together or apart would depend upon the injury being treated, the length of the treatment, and the condition of the patient. The administration of leupeptin can be either parenteral during and after surgical procedures, or in an oral form for longer term treatment. Depending upon the condition of the patient, the administration of these compounds together or separately would obviously depend upon

multiple criteria and would have been common decisions for one of ordinary skill in the art at the time of the invention.

A mixture of these compounds would have been obvious to one of ordinary skill in the art at the time of the inventions for the reasons stated above, and the mixtures properties and administration would obviously be dependent upon the properties of each individual component in the mixture. In the instant case (protease inhibitors) are known to be more efficacious upon rapid delivery to the injured site, and it would have been obvious to one of ordinary skill in the art at the time of the invention, that the inclusion of this compound would necessitate administration methods which would include its administration in a rapid manner. The systemic or proximal administration of the protease inhibitor (leupeptin/aminobenzamide) was also known, which would effect the administration of the mixture of compounds as well. Depending upon the condition of the patient, the administration of these compounds would obviously depend upon multiple criteria and would have been common decisions for one of ordinary skill in the art at the time of the invention.

Regarding the wherein clause drawn to treating injuries caused by hydrocephaluss, the article of Del Bigio provides provides evidence that hydrocephalus causes nerve damage to the brain due to ischemic injury which is treated by the calcium channel blocker nimodipine through improved blood flow, prevention of calcium influx, or proteolytic process mediation. (See the abstract.) As hydrocephalus causes injury to nerves it would have been obvious to treat nerve injuries and the pain associated with

such injuries using the methods of Berde and Stracher Travis, Saidi, and Josephson that were taught above.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LANCE RIDER whose telephone number is (571)270-1337. The examiner can normally be reached on M-F 11-12 and 1-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LANCE RIDER/
Examiner, Art Unit 1618

/Jake M. Vu/
Primary Examiner, Art Unit 1618